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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,450	02/11/2004	Wesley K.M. Chong	PC19074	3704

28940 7590 05/16/2005

AGOURON PHARMACEUTICALS, INC.
10350 NORTH TORREY PINES ROAD
LA JOLLA, CA 92037

EXAMINER

LEE, SUSANNAH E

ART UNIT PAPER NUMBER

1626

DATE MAILED: 05/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/776,450

Applicant(s)

CHONG ET AL.

Examiner

Susannah Lee

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) 7-9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/22/04</u> . | 6) <input type="checkbox"/> Other: _____ |

S.O.O.

DETAILED ACTION

Claims 1-9 are pending in the instant application. Claims 7-9 are withdrawn by Applicant.

Priority

This application claims benefit of provisional application number 60/447,329, filed on 02/12/2003.

Response to Non-Final Office Action

Amendment of Claims

Acknowledgment is made of applicant's amendment of the claims filed on 04/04/2005.

Confirmation of Election/Restriction

Applicant's confirmation of the election of Group I, Claims 1-8, without traverse is acknowledged.

Examiner's 35 USC 103 Rejection

Applicant disagrees with Examiner's 35 USC 103 rejection because "Applicants submit that the Examiner has failed to point to any motivation or suggestion in the prior art to replace the carbonyl with the elaborated sulfonyl and sulfonamide groups of the present invention." (Applicant's Remarks, page 154, lines 30-32).

Examiner respectfully disagrees with Applicant and will maintain the rejection of Claims 1-6 under 35 U.S.C. 103(a) because the Chong reference does provide the requisite motivation to make the instantly elected/claimed compounds (see analysis below). This rejection is set forth in a prior Office Action, mailed on 11/29/2004.

Examiner's 35 USC 112 Rejection

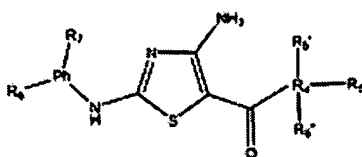
Examiner's 35 USC 112 rejection is withdrawn in light of the amendment to the claims filed on 04/04/2005, where Applicant deletes "prodrug or pharmaceutically active metabolite of a compound of


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the Formula (I) or pharmaceutically acceptable salt.” (see Amendments to the Claims, filed on 04/04/2005, pages 4, 6, 8, 10, and 12).

Scope of the Elected Invention

Claims 1-9 are pending in this application. The scope of the invention of the elected subject matter is as follows:



Compounds of formula, (m), depicted in claim 2, wherein: R₄ is C2-C14 alkyl, C3-C10cycloalkyl, or aryl, R₅ is hydroxyl, halo, C1-C14 alkyl, C1-C14 alkoxy, acyl, R_{5'} and R_{5''} are hydrogen, hydroxyl, halo, C1-14 alkyl, C1-14 alkoxy, acyl, R₆ is , R₇ is hydrogen, hydroxyl, halo, C1-C14 alkyl, C1-14 alkoxy, acyl; and R₉ is hydrogen, C1-C9 alkyl, C2-C9 alkenyl, 2-9 membered heteroalkenyl, C1C9 alkylamide, C1-C9 alkyl-carboxamide, C1-C4 alkyl-cycloalkyl, C1-C4 alkyl-aryl, C3-C10 cycloalkyl, and aryl.

Scope of Withdrawn Subject Matter

Claims 1-6 (in part) and 7-9 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

As a result of the election, Claims 1-6 (in part) are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions. The withdrawn compounds contain varying core structures, such as pyrimidinyl, piperidinyl, imidazolyl, pyrrolidinyl, etc., which are chemically recognized to differ in structure and function. This recognized chemical diversity of the functional groups can be seen by the various classifications of these functional groups in the U.S. Classification System. For instance, thiazoles are in various subclasses of class 548 and the heteroaryl moieties are in various subclasses of classes 544 (pyrimidines), 546 (pyridines), 548 (indoles), and 549

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(thiophenes). Therefore the subject matter which are withdrawn from consideration as being non-elected subject matter differ materially in structure and composition and have been restricted properly.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

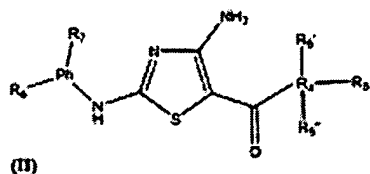
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.


Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chong et al., U.S. Pat. No. 6,569,878.

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Applicants instant elected invention teaches the compound of formula,

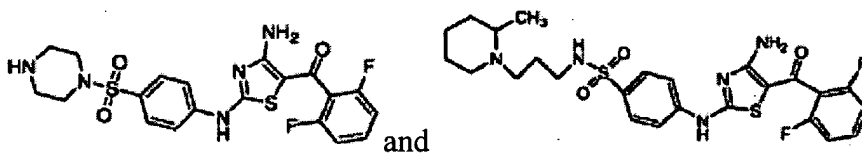


, depicted in claim 5 and their multimers, wherein: R₄ is phenyl, R₅ is H,

R_{5'} and R_{5''} are F, R₆ is , R₇ is hydrogen; and R₉ is C1-C9 alkyl, 2-9 membered

heteroalkenylC1-C4 alkyl-heteroaryl, and 3-10 membered heteroaryl, yielding the compounds depicted

in claim 5, page 10, line 2 and 9,

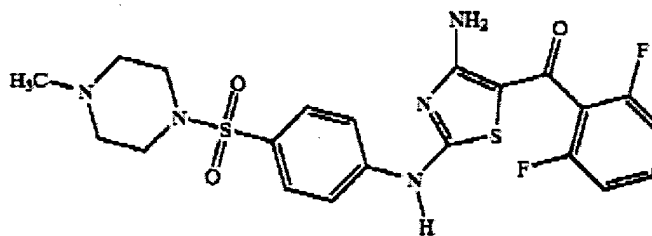


and

These products, according to claims 8 and 9, page 13, lines 5-9, can be used for treating cellular proliferative diseases, cancer, autoimmune disease, viral disease, fungal disease, neurodegenerative disorder or cardiovascular disease.

Determination of the scope and content of the prior art (MPEP § 2141.01)

Chong teaches diamino substituted thiazole compounds and the pharmaceutically acceptable

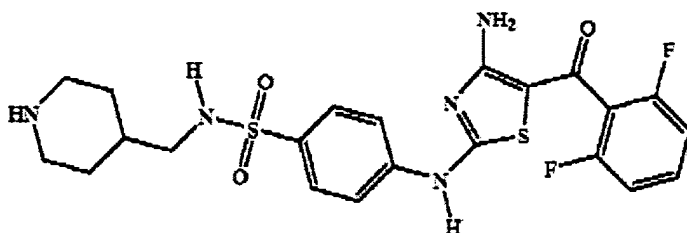


salts thereof depicted by the formula,

or {4-

Amino-2-[4-(4-methyl-piperazine-1-sulfonyl)-phenylamino]-thiazol-5-yl}-(2,6-difluoro-phenyl)-methanone, (See Pat. No. 6,569,878, Columns 95 and 193, Example C(116));

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or 4-[4-Amino-5-(2,6-difluoro-benzoyl)-

thiazol-2-ylamino]-N-piperidin-4-ylmethyl-benzenesulfonamide, (See Pat. No. 6,569,878, Columns 124 and 193, Example J(4)). These products can be used to alleviate the symptoms of cellular proliferative diseases and cancer (Column 3, lines 29-43).

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the prior art of Chong and the instantly claimed compounds is a methyl versus hydrogen group. There are two species that are claimed in the instant application that are taught in Chong. In the first example, Chong teaches a 4-methyl-piperazine group off the sulfonyl group, while the instant application discloses a piperazine group. The difference being a hydrogen instead of a methyl at the 4 position of the piperazine ring in the instant application. In the second example, Chong teaches a piperidine group off the sulfonyl group, while the instant application discloses 2-methyl-piperidine. The difference being a methyl instead of a hydrogen at the 2 position of the piperidine ring in the instant application.

Finding of prima facie obviousness – rationale and motivation (MPEP § 2142-2413)

However, in the absence of showing unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with Chong et al. to make products that are useful for the treatment of cellular proliferative diseases and cancer, wherein methyl and hydrogen are interchangeable.

In the first example noted above, Chong teaches a tertiary amine and the instant application discloses a secondary amine. This is an obvious variant. The interchange of alkyl and hydrogen is

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obvious in and of itself. Secondary and tertiary amines are interchangeable. Ex parte Bluestone, 135 USPQ 199.

In the second example, Chong teaches a hydrogen substituent off the piperidine ring, while the instant application discloses a methyl substituent. Hydrogen and methyl are deemed obvious variants. In re Wood, 199 USPQ 137.

The motivation would be to prepare similar compounds pharmacologically active against cellular proliferative diseases and cancer. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with Chong et al. to make products that are useful for the treatment of cellular proliferative diseases and cancer, wherein methyl and hydrogen are interchangeable.

Obviousness Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

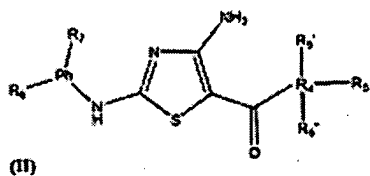
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).


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Claims 1-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-14 of U.S. Patent Num. 6,569,878 ('878 Patent).

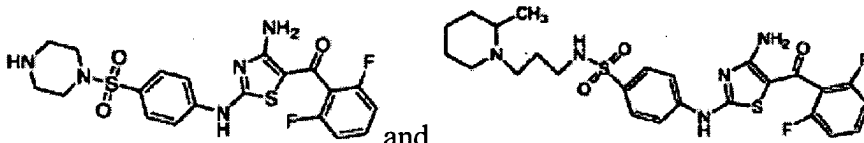
Applicants instant elected invention teaches the compound of formula,



, depicted in claim 5 and their multimers, wherein: R₄ is phenyl, R₅ is H,

R_{5'} and R_{5''} are F, R₆ is , R₇ is hydrogen; and R₉ is C1-C9 alkyl, 2-9 membered heteroalkenyl, C1-C4 alkyl-heteroaryl, and 3-10 membered heteroaryl, yielding the compounds depicted

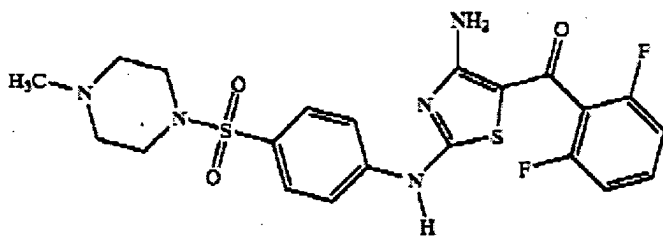
in claim 5, page 10, line 2 and 9,



These products, according to claims 8 and 9, page 13, lines 5-9, can be used for treating cellular proliferative diseases, cancer, autoimmune disease, viral disease, fungal disease, neurodegenerative disorder or cardiovascular disease.

Determination of the scope and content of the prior art (MPEP § 2141.01)

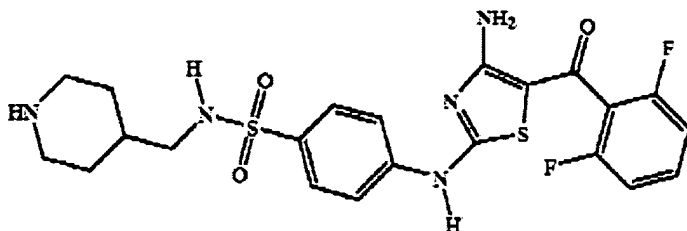
'878 Patent teaches diamino substituted thiazole compounds and the pharmaceutically acceptable salts thereof depicted by the formula,



or {4-Amino-2-[4-(4-methyl-piperazine-1-

sulfonyl)-phenylamino]-thiazol-5-yl}-(2,6-difluoro-phenyl)-methanone, (See Pat. No. 6,569,878, Columns 95 and 193, Example C(116));

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or 4-[4-Amino-5-(2,6-difluoro-benzoyl)-

thiazol-2-ylamino]-N-piperidin-4-ylmethyl-benzenesulfonamide, (See Pat. No. 6,569,878, Columns 124 and 193, Example J(4)). These products can be used to alleviate the symptoms of cellular proliferative diseases and cancer (Column 3, lines 29-43).

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the '878 Patent and the instantly claimed compounds is a methyl versus hydrogen group. There are two species that are claimed in the instant application that are taught in the '878 Patent. In the first example, the '878 Patent teaches a 4-methyl-piperazine group off the sulfonyl group, while the instant application discloses a piperazine group. The difference being a hydrogen instead of a methyl at the 4 position of the piperazine ring in the instant application. In the second example, the '878 Patent teaches a piperidine group off the sulfonyl group, while the instant application discloses 2-methyl-piperidine. The difference being a methyl instead of a hydrogen at the 2 position of the piperidine ring in the instant application.

Finding of prima facie obviousness – rationale and motivation (MPEP § 2142-2413)

However, in the absence of showing unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with the '878 Patent to make products that are useful for the treatment of cellular proliferative diseases and cancer, wherein methyl and hydrogen are interchangeable.

In the first example noted above, the '878 Patent teaches a tertiary amine and the instant application discloses a secondary amine. This is an obvious variant. The interchange of alkyl and

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hydrogen is obvious in and of itself. Secondary and tertiary amines are interchangeable. Ex parte Bluestone, 135 USPQ 199.

In the second example, the '878 Patent teaches a hydrogen substituent off the piperidine ring, while the instant application discloses a methyl substituent. Hydrogen and methyl are deemed obvious variants. In re Wood, 199 USPQ 137.

The motivation would be to prepare similar compounds pharmacologically active against cellular proliferative diseases and cancer. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with the '878 Patent to make products that are useful for the treatment of cellular proliferative diseases and cancer, wherein methyl and hydrogen are interchangeable.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, Claim 1 is indefinite because the R6 moiety is not defined. Claim 1 discloses that "R6 is a group selected from the following formulae: wherein, etc...." The substituents of R6 are missing therefore the claim is indefinite. The substituents of R6 must be inserted after the word "formulae:" to overcome this rejection.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the

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mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Lee whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susannah Lee
Patent Examiner, AU 1626

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

for

Kamal Saeed
Joseph K. McKane
Supervisory Patent Examiner
AU 1626
Date: 05/10/05